THE INFLUENCE OF IONISABLE GROUPS ON THE ROTATORY POWER OF OPTICALLY ACTIVE OCTYL AND MENTHYL ESTERS.

Thesis for the Degree of Doctor of Philosophy.

by

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There is little doubt that, as was first suggested in 1870 by van 't Hoff and Le Bel independently, a definite connection exists between the optical activity and the chemical constitution of a compound. Several attempts have been made to formulate a quantitative relationship between the optical rotatory power of a substance and the properties of the groups attached to the asymmetric atom. Guye (Compt. rend.,1890,110, 1724; 1893,116,1378,1451) calculated the degree of asymmetry from the relative masses of the four radicals grouped round the asymmetric carbon atom and the distances of their centres of gravity from the asymmetric atom. This theory held approximately for the variations due to alkyl groups in certain series of esters. It failed, however, under more searching examination. Crum Brown (Proc.Roy.Soc.Edin., 1890,182) gave to each radical a value K which was a function of the composition and constitution of the radical. So far K possesses no great significance as it has not yet been found possible to calculate it for any radical. Later investigators have concerned themselves with attempts to obtain regularities of different types in optically active substances.

An interesting regularity in certain lactones derived from acids of the sugar group was established /

established by Hudson (J.A.C.S.,1910,32,338). He showed that in the case of lactones having a five atom ring structure, where the oxide ring of the lactone was formed by engaging a γ-CHOH group of the dextro-configuration the rotation was increased in the dextro sense, the reverse also holding. Haworth extends this rule to lactones and sugars having a six atom ring structure. Haller and Desfontaines (Compt. Rend., 1905,140,1205) showed that an increase in rotatory power due to ring formation is observed chiefly when the asymmetric atom is a part of the ring system.

Frankland (J.C.S.,1912,101,658), in studying homologous series found that the rotatory powers of the first members of the series are low but that in the later members the values rise rapidly to a constant. This regularity may however be modified if there are other chemically active groupings near the asymmetric centre. For example, Hilditch (J.C.S.,1912,101,192) concludes that when one unsaturated group is present in a homologous series there is a definite "series constant" for that series, but when there is more than one unsaturated group near the active atom there is no noticeable regularity. Comparing unsaturated with saturated homologous series, Christopher and Hilditch (J.C.S.,1912,101,202) show, in the menthyl esters of the α-bromo-aliphatic acids, that in the saturated esters there is a rapid rise to

a/

a constant value, but in those containing an unsaturated group there are two effects acting, and that the result is an enhanced rotation in the early members followed by a rapid fall and slight rise to a constant value in the later members. The comparative effects of different halogens as substituent groupings have been examined by a number of investigators including Cohen (J.C.S., 1911, 99, 1061). The latter obtains the following figures for the menthyl esters of the acids indicated below:

	Acetic	Iodoacetic	Bromacetic	Chloracetic
$[M]_D^{100°}$	-151.5	-154.3	-168.3	-169.7

	Dichloracetic	Trichloracetic
$[M]_D^{100°}$	-163.2	-177.3

	-Iodopropionic	-Chloropropionic	-Chloropropionic
$[M]_D^{100°}$	-142.2	-153.1	-145.0

	-Bromopropionic
$[M]_D^{100°}$	-155.2

	Phenylacetic	Phenylbromacetic	Phenylchloracetic
$[M]_D^{100°}$	179.6	185.7	190.5

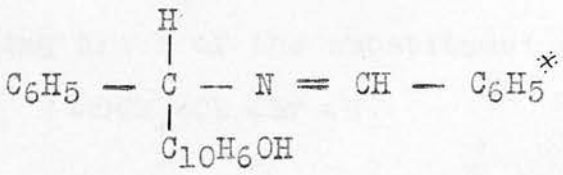
These figures show clearly that substitution by a halogen increases the rotatory power of a compound, and that, although the regularity is not great, the values, on the whole, point to the relative effects

Cl > Br > I > H

Recent researches on the rotatory powers of derivatives/

derivatives of optically active alcohols indicate that there are at least two types of substituent effect. Among esters of the straight chain aliphatic acids it has been shown that the influence of a number of simple substituents agrees more or less closely with their influence on acidity, reaction velocity, and molecular inductive capacity. The series of substituting groups so obtained is known as the general polar series. A theoretical basis for this series has been established as a development of the attempt made by J. J. Thomson (Phil.Mag.,1923,(VI),46, 497) to explain orientation effects in benzene substitution. Thomson considered that the substituent groups NO_2 and COOH could be represented as electrical doublets arranged in an opposite sense to those representing Cl, OH, and CH_3. Later work by Errara (Compt.rend.,1926,182,1623) and Höjendahl (Nature,1926, 117,892) on the relationship between dipole moment and molecular structure shows that, in all probability, CH_3 and NH_2 are electropositive groups of one orientation and that NO_2, COOH, Cl, OCH_3 are electronegative groups oriented in the opposite sense.

The general polar effect of substituents in optically active compounds is evident in the large number of Schiff's bases of the type



examined by Betti (Gazzetta Chimica Italiana,1923,53 417). In these compounds the phenyl group marked * had one or more substituents attached to the nucleus. Arranging the different substituents in order of their effect on the rotation of the parent compound, Betti finds that the series so obtained agrees very closely with that representing the relative strengths of the benzoic acids $C_6H_4X.COOH$ corresponding to the aldehydes from which the Schiff's bases were prepared. Rule and Smith (J.C.S.,1925,127,2188) examined the rotatory powers of menthyl esters of the type

$$X - CH_2 - COOC_{10}H_{19}$$

where X = CN,COOH, OH, OCH_3 or OC_2H_5

They concluded that the relative effect of a number of substituents could be represented by the following series

$$CN > Cl > Br > OH > OCH_3 > CH_3 > COOH > H,$$

and that this is closely analogous to the general polar series as deduced from the molecular inductive capacity of benzene derivatives or the acidity of the substituted acetic acids. Rule and Mitchell (J.C.S., 1926,3202) found that the agreement is less satisfactory in the corresponding sec-β-octyl esters. They examined the octyl esters of methoxy, chloro, bromo, and iodoacetic acids and found that their results gave the following order of the substituent groups

$$H < OCH_3 < Cl < Br < I.$$

The/

The general polar series derived from acidities has the order

$$H < OCH_3 < I < Br < Cl$$

The second type of substituent effect has been observed chiefly among active menthyl and octyl esters of ortho-substituted acids of aromatic type. Cohen examined numerous menthyl esters of substituted benzoic acids and found that his results could not be explained on the basis of Frankland's lever arm theory, which gives the order o < unsubst. < m < p. Cohen confirmed Tschugaeff's earlier conclusion that the element or group nearest the optically active atom has the greatest effect, whether in raising or in lowering the rotatory power.

Rule (J.C.S.,1924,125,1121) has pointed out that among the ortho-substituted esters a meta directive substituent raises the rotatory power and one of ortho and para directive type lowers the value. The actual magnitude of the changes produced agrees closely with the orienting powers of the substituents as deduced from the proportion of meta or ortho and para derivatives formed on nitrating the corresponding substituted benzenes. The rotatory powers of naphthyliminocamphors and derivatives of phenylimino-camphor have been studied by Singh and Mazumder, (J.C.S.,1919,105, 566) who find that their results do not agree with Frankland's or Cohen's conclusions.

They/

They find that, using either chloroform or methyl alcohol as solvent, their results can be arranged as follows

ortho substitution	$Cl < OCH_3 < CH_3 < Br < H$
meta substitution	$Cl = Br < CH_3 < H$
para substitution	$Br < H < Cl < CH_3 < OCH_3$

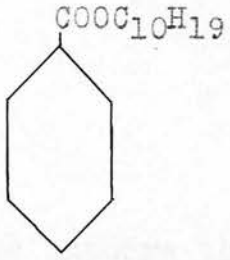
In this case the o-series is in quantitative agreement with that obtained for the menthyl esters of ortho-substituted benzoic acids, the o,p-directive groupings lowering the rotation.

On the basis of the above analogy with benzene substitution, Rule,(J.C.S.,1927,54) concludes that there should be pronounced changes in rotatory power when the substituent groupings are ionisable. It is known that an ionised complex exerts a powerful influence on substitution in the benzene nucleus, the course of this reaction varying with the sign of the charge. Thus aniline ordinarily substitutes in the ortho and para positions but may be nitrated in the meta position by using it as the sulphate in presence of a large excess of sulphuric acid. The ionic complex $.NH_3^+$ thus behaves as a meta directive substituent. Benzoic acid, which brominates slowly in the meta position, can be converted rapidly into the ortho and para substituted compounds by chlorinating the sodium salt in aqueous solution. The complex $CO.O^-$ is therefore ortho and para directive. The rotatory/

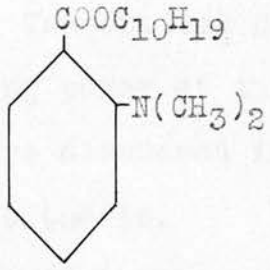
rotatory powers of simple active acids and bases frequently undergo a reversal of sign when the compounds are ionised. This can be explained as in the above cases especially if the acidic or basic group is/only highly polar one present, as in lactic, glyceric and methoxysuccinic acids, and the phenylpropyl acetic acid prepared by Pickard and Yates (J.C.S.,1909,95,1011). The sodium salt of valeric acid has been found by Rule to have a greatly diminished rotatory power when compared with that of the free acid. The substituted optically active sulphoxides prepared by Harrison,Kenyon and Phillips (J.C.S.,1926,2079) also have diminished rotatory power or actually change sign on ionisation. In the last examples the ionisable groups are separated from the asymmetric sulphur atom by a benzene nucleus. Additional support is found in the variations of the rotatory powers of active amino acids in alkaline, neutral and acid solution. The amino acid in aqueous solution is only slightly ionised, in alkaline solution the carboxyl group is ionised, and in acid solution ionisation takes place in the amino group. The changes of rotatory power correspond, in many cases, to these changes in condition.(Rule,loc.cit.)

The menthyl esters of hydroxy, amino, and dimethylaminobenzoic acids have been prepared by Rule/

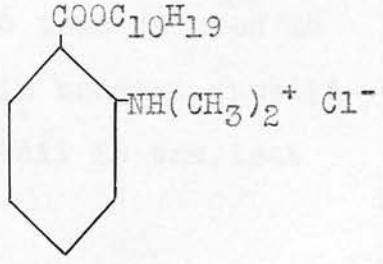
Rule and MacGillivray (J.C.S.,1929,401) who find that the ortho derivatives differ considerably in rotatory power from the unsubstituted ester. In these compounds the introduction of an ortho-carboxyl group causes a considerable rise in the rotatory power which changes to a fall when the substituent is ionised to $.CO.O^-$. On the other hand an orthodimethyl amino group depresses the rotatory power, which rises on ionisation to $N.(CH_3)_2H^+$. The actual values they obtained in alcoholic solution are as follows:-



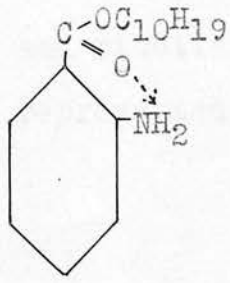
$[M]_{5461}$ -275.1°



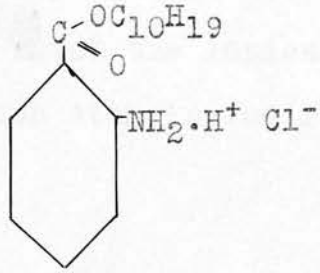
$[M]_{5461}$ -250°



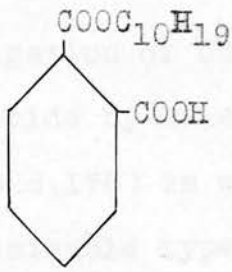
-292°

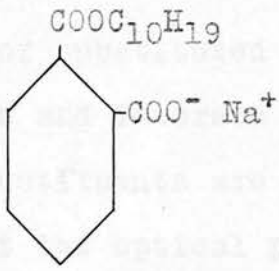


$[M]_{5461}$ -313°

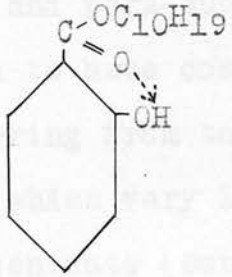


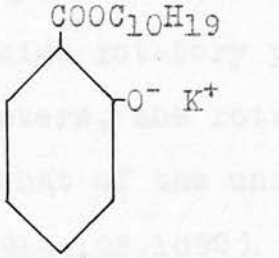
-292°





$[M]_{5461}$ -345.6° -260.5°





$[M]_{5461}$ -299° -246°

It is suggested by these authors that the high rotations of the free ortho-aminobenzoic and salicylic esters are due to the compounds existing in a chelated state. The optical changes are thus related to the orienting power of the groups in benzene substitution and are discussed in more detail in the last part of this thesis.

The following thesis deals with the sec-β-octyl esters of hydroxy, amino, and dimethylaminobenzoic acids and the menthyl and octyl esters of quinaldinic and picolinic acids in which the ionisable grouping is represented by a nitrogen atom in the ring.

An/

An investigation of octyl esters of substituted benzoic acids by Rule, Hay, Numbers and Paterson (J.C.S., 1928, 178) in which the substituents are of the non-ionisable type showed that the optical properties of the ortho substituted esters were similar to those of the corresponding menthyl derivatives. The meta- and para-substituted octyl esters, however, were found to have comparatively high rotatory powers, thus differing from the menthyl esters, the rotatory powers of which vary little from that of the unsubstituted benzoate (Cohen, J.C.S., 1914, 105, 1892).

$[M]_D^{20}$ ortho-Substituted Esters.

Substituent	l-octyl	l-Menthyl
NO_2	-122°	-381°
COOH	90 - 117	332
H	77.8	239
CH_3	68.1	231
I	44.3	237
Br	49.2	205
Cl	47.1	195
OCH_3	33.0	148

para/

$[M]_D^{20}$ para-Substituted Esters.

Substituent	1-Octyl	1-Menthyl
NO	-119.7°	-237.5°
OCH	113.3	≈39 $[M]_D^{100}$
Cl	103.6	≈37
CH	103.5	≈37 $[M]_D^{100}$
H	77.8	≈39 $[M]_D^{20}$ − 233 $[M]_D^{100}$

In the case of the amino and hydroxy esters the methods of preparation used by Rule and MacGillivray were conversion to the acid chloride by means of thionyl chloride followed by the heating of the acid chloride with menthol. The amino esters were obtained by reduction of the corresponding nitro-esters. The yields obtained varied but except in the case of the ortho-compounds were very low. Owing to the much greater difficulty of obtaining active octyl alcohol as compared with menthol, and the comparatively large quantities required owing to the probable small yields, the above methods were not considered satisfactory. The method used in the preparation of most of the following octyl esters consists in heating molecular proportions of octyl alcohol and of the methyl ester of the required acid with a twentieth of an atomic proportion of metallic sodium/

sodium. This method which is mentioned by Verley (Bull.Soc.Chim.,1927,41,802) is described in detail in the experimental part of this thesis.

EXPERIMENTAL.

The octyl alcohol used for the following preparations was obtained from the racemic form by the method described by Pickard and Kenyon (J.C.S., 1907,2058; 1922,2540). The octyl hydrogen phthalate had a rotatory power $[\alpha]^{15°}_{5461} \pm 58.3$ - $\pm 58.5°$ (in alcohol, c = 5), and the homogeneous octyl alcohol $\alpha^{17}_{5461} \doteq \pm 9.4°$. The menthol used had a rotatory power $[\alpha]_D = -49.75$ in alcoholic solution (c = 10).

d-sec-β-Octyl o-Dimethylamino-benzoate.

Methyl o-dimethylamino-benzoate was prepared in the usual manner starting from methyl alcohol and o-dimethylamino-benzoic acid and using hydrochloric acid as a catalyst.

d-Octyl alcohol (16 gm.) was placed in a 100 c.c. distilling flask connected to a condenser and provided with a cork bearing a capillary tube. The latter was connected at its outer end to a calcium chloride drying tube so that dry air could be drawn through the apparatus. The octyl alcohol was treated with sodium (0.2 gm.) and heated until complete solution of the metal occurred. Methyl o-dimethylamino-benzoate (23 gm.) was then added and the mixture was heated at 130°C for 8 hours. (In later experiments this was reduced to 3 - 4 hours). The pressure was reduced slightly and a current of dry air was drawn through the liquid in order to remove methyl alcohol from the mixture and thus enable the action, which is a balanced one, to become displaced as far as possible in favour of the octyl ester. The semi-liquid mixture was extracted with ether and the ether solution washed well with sodium bicarbonate solution and finally with water. The solution was dried/

dried over anhydrous sodium sulphate and , after removal of ether, the residue was distilled under diminished pressure. The fraction distilling at 126°C under 0.2 mm. was retained and after two additional fractionations its rotatory power in the homogeneous state was found to be constant. Yield of pure ester, 8 gm.

The pure ester was an odourless slightly yellow liquid having a violet fluorescence. It was soluble in dilute hydrochloric acid.

Analysis: (by Dumas' method)

0.2129 gm. of ester gave 9.4 c.c. Nitrogen at 15.5°C and 751.6 mm. pressure

Found N = 5.17%

$C_{17}H_{27}O_2N$ requires N = 5.05%

Density determination:

A density determination was made at 17°C using a pyknometer holding about 1.5 c.c.

Weight of water 1.5553 gm.

Weight of ester 1.5222 gm.

Density of Ester $D_4^{17°}$ = 0.9772

Rotatory power:

The following page contains the rotations observed in various solvents at the temperatures and concentrations/

concentrations indicated, and the molecular rotations calculated from them. No value was obtainable for the mercury violet line λ_{4358} in the case of the homogeneous ester owing to adsorption.

Rotatory power of d-Octyl o-Dimethylamino-benzoate.(M.W. 277.2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Homogeneous	0.5	17	(D= .9772)	+4.08	+4.96	+5.65	–	+23.2	+28.1	+32.1	–
Ethyl Alcohol	2	16	5.112	+0.89	+1.09	+1.17	+0.45	+24.1	+29.6	+31.7	+12.2
Methyl Alcohol	1	14	4.714	–	–	+0.46	+0.08	–	–	+27.1	+4.7
Ethyl Alcohol + 1 molecular proportion of HCl	1	15	4.975	+0.86	+1.04	+1.23	+2.14	+47.9	+57.9	+68.5	+119.0
Ethyl Alcohol + 2 molecular proportions of HCl	1	16	4.993	–	–	+1.26	–	–	–	+70.0	–
Ethyl Alcohol + 4 molecular proportions of HCl	1	16	5.161	–	–	+1.32	–	–	–	+70.9	–

d -sec-β-Octyl p-Dimethylamino-benzoate.

This compound was prepared by the method employed for the corresponding ortho ester, using 0.2 gm. sodium, 25 gm. methyl p-dimethylamino-benzoate and 17 gm. octyl alcohol. On distillation, the fraction boiling at 180°C under 1.8 mm. was retained. Three fractionations were necessary before the rotation of the homogeneous ester was found constant. Yield of pure ester 16 gm.

The pure ester was an odourless, pale yellow liquid having a violet fluorescence. It was soluble in dilute hydrochloric acid.

Analysis:

Considerable difficulty was met with in analysing this ester for nitrogen by the Dumas method, the values being variable and very high. It was found later that this was due to the nitrogen being mixed with an inflammable gas, probably methane or ethane. A modified Dumas analysis (cf. Haas, J.C.S., 1906, 89, 570) using cuprous chloride and potassium bichromate in the tube as well as copper oxide also gave too high a result. Ter Meulen's hydrogenation method was tried and gave the correct result.

.0861 gm. of ester required 5.37 c.c. of .0574 N Acid (HCl) to neutralise the ammonia it produced.

Found N = 5.02%

$C_{17}H_{27}O_2N$ requires N = 5.05%

Density determination:

Density values were obtained at 16°C by means of a pyknometer holding about 1 c.c.

Weight of water (1) 1.0745 gm.

(2) I.0743 gm.

Weight of ester (1) 1.0646 gm.

(2) I.0644 gm.

Density $D_4^{16°}$ (1) 0.9897 (2) 0.9897

Rotatory power:

The succeeding page contains a table of observed and molecular rotations.

Rotatory power of d-Octyl p-Dimethylamino-benzoate (M.W. = 277.2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Homogeneous	0.5	16	(D= .9897)	+20.36	+27.9	+34.07	+66.40 ※	+114.1	+156.4	+190.9	+372.0
Ethyl Alcohol	2	17	5.069	+ 4.79	+ 6.35	+ 7.80	+15.76	+131	+174.0	+213.0	+431.0
Ethyl Alcohol + 1 molecular proportion of HCl	2	16	5.009	+ 3.24	+ 4.43	+ 5.31	+ 9.79	+ 89.7	+123.0	+147.0	+271.0

※ Owing to absorption of the violet light this value is only an approximation.

l-sec- β -Octyl Anthranilate.

The methyl anthranilate used was obtained from British Drug Houses,Ltd. It melted at 25°C (Richter's Lexikon,1913, quotes 25.5°). The octyl ester was prepared in the same way as the corresponding dimethylamino-benzoate except that the time of heating was reduced to 3 hours. The quantities used were 0.2 gm. sodium, 23 gm. methyl anthranilate and 20 gm. octyl alcohol. After distillation under diminished pressure two additional fractionations were found necessary to obtain a constant rotation for the homogeneous ester. The ester boiled at 18_3°C under 12 mm. Yield of pure ester 10 gm.

The pure ester was pale yellow in colour and practically odourless. It had a pronounced violet fluorescence. With hydrochloric acid it gave a solid hydrochloride.

Analysis: (by Dumas's method)

0.2359 gm. ester gave 11.5 c.c.Nitrogen at 13°C and 764.5 mm. pressure

Found N = 5. 84%

$C_{15}H_{23}O_2N$ requires N = 5.62%

Rotatory power/

Rotatory power:

The following page contains a table of observed and molecular rotations.

The residual ester was hydrolysed by heating with alkali and the rotation of the recovered octyl alcohol observed (see page 49).

Rotatory power of l-Octyl Anthranilate (M.W. 249·2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	17·5	6·033	−0·60	−0·56	−0·50	+1·63	−25	−23	−21	+67
Ethyl Alcohol + 1 molecular proportion of HCl	2	14·5	5·517	−1·85	−2·42	−2·82	−4·33	−41·8	−54·7	−63·7	−97·9

l-sec-β-Octyl m-Amino-benzoate.

The preparation of this ester was attempted by the sodium catalytic method but owing to decomposition the yield obtained (3 gm. from 16 gm. of octyl alcohol and 18 gm. methyl m-aminobenzoate) was too small for purification. The dark brown residue remaining in the flask after distillation solidified on cooling. It was slightly acid to litmus and was readily soluble in alcohol and slightly so in ether.

The method used by Rule and MacGillivray (J.C.S.,1929,401) for the preparation of menthyl o-, m-, and p-amino-benzoates was therefore tried.

Octyl m-Nitrobenzoate.

This compound was prepared by the method used by Rule and Numbers (J.C.S., 1926,2116). The ester used had $\alpha_{5461} = 24.98$ ($l = .5$) in the homogeneous state (Rule and Numbers quote $\alpha_{5461} = 24.88$).

Octyl m-Amino-benzoate.

Reduction of the m-nitroester was attempted using titanous chloride as reducing agent but this method was not successful owing to hydrolysis. A method recommended by Houben Weyl (vol.2,page 325) for the reduction of nitro-esters to amino-esters was next tried. The reducing agent in this case was aluminium amalgam which was prepared according to the method/

method given by Wislicenus (Jour.f.prakt.Chem., [2], 54, 55). The reduction was carried out in exactly the same manner as was used to reduce methyl m-nitro-p-hydroxybenzoate by Auwers and Rohrig (Ber., 1897, 30, 989) except that a double quantity of the aluminium amalgam was used. After four hours heating the solution was filtered clear from aluminium and aluminium hydroxide. The alcohol and water were distilled off and the residue taken up in ether. The ether solution was dried over anhydrous sodium sulphate and, after removal of the ether, the residue was distilled under diminished pressure. A liquid boiling at 195 - 198° under 18mm. was collected. Slight decomposition appeared to take place during the distillation and the ester was not further fractionated. Yield 5 gm. from 16 gm. nitro-ester. Unsuccessful attempts to obtain a solid derivative (picrate, trinitrobenzene derivative, hydrochloride) were also made. The ester was a pale yellow liquid. There was no evidence of octyl alcohol being produced as a result of the decomposition.

Analysis: (by Ter Meulen's hydrogenation)

0.0658 gm. of ester required 4.36 c.c. of .0574 N hydrochloric acid to neutralise the ammonia it produced.

Found N = 5.33%

$C_{15}H_{23}O_2N$ requires N = 5.62%

Although this method tends to produce low analytical results it is possible that the ester was not absolutely pure. The figures for rotatory power given below should however, indicate the correct direction of change on ionisation.

Rotatory power.

The succeeding page contains tables of observed and molecular rotations in the solvents and at the temperature and concentrations indicated.

Rotatory power of *l*-Octyl m-Amino-benzoate (M.W. = 249·2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	17·5	6·391	-2·38	-2·77	-3·10	-5·79	-92·8	-108	-121	-226
Ethyl Alcohol + 1 Molecular proportion of HCl	1	18	6·16	-1·91	-2·53	-2·93	-2·52* (l=0·5)	-77·3	-102	-119	-204

* Owing to absorption of the violet light by the ester this value had to be obtained in a tube 0·5 dcm. in length and is only an approximation.

l-sec- β-Octyl p-Amino-benzoate.

This compound was prepared using 0.2 gm. sodium 18 gm. octyl alcohol and 20 gm. methyl p-amino-benzoate. The methyl amino-benzoate was obtained from British Drug Houses, Ltd., and recrystallised from petrol ether (60 - 80°) until pure. On fractionation of the crude octyl ester a liquid boiling at approximately 200°C under 10 mm. was obtained. The liquid solidified to a white solid on cooling. Four recrystallisations from petrol ether (40 - 60°) were necessary before the rotation of the substance in 5% alcoholic solution was constant. Yield of pure ester 7 gm.

The ester was an odourless, white, flaky solid melting at 69-70°C to a colourless liquid. The hydrochloride, which was prepared by warming with excess hydrochloric acid and evaporating to dryness in vacuo, melted at 131-133°C.

Analysis: (By Ter Meulen's hydrogenation)

.0665 gm. of ester required 4.67 c.c. of .0574 N. Hydrochloric acid to neutralise the ammonia it produced.

Found N = 5.64%

$C_{15}H_{23}O_2N$ required N = 5.62%

Rotatory power:

Tables of observed and molecular rotations are on the page following.

Rotatory power of *l*-Octyl p-Amino-benzoate M.W. = 249·2.

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	17·5	4·317	-1·85	-2·33	-2·82	-5·52	-107	-134	-168	-319
Ethyl Alcohol + 1 molecular proportion of HCl	1	14	4·051	-1·37	-1·56	-1·77	-3·45	-84·3	-96·0	-109	-212

d-sec-β-Octyl Salicylate.

This compound was prepared in the same way as octyl anthranilate except that dilute hydrochloric acid was used as a washing agent in place of dilute alkali. The quantities used were 0.2 gm. sodium, 23 gm. methyl salicylate and 20 gm. octyl alcohol. Three fractionations were necessary for purification. The boiling point of the final fraction was 170°C under 10 mm. pressure. The pure ester was an odourless and colourless liquid, which was miscible with organic solvents. Yield of pure ester 14 gm.

Analysis:

0.1476 gm. ester gave 0.1277 gm. water and 0.4169 gm. carbon dioxide.

Found C = 71.87%, and H = 9.05%

$C_{15}H_{22}O_3$ requires C = 71.93% and H = 8.79%.

Density determinations:

Density values were obtained at 18°C by means of a pyknometer holding about 1 c.c.

Weight of water 1.0738 gm.

Weight of ester (1) 1.0843 gm., (2) 1.0838 gm.

Density of ester $D_4^{18°}$ 1.0085

(2) 1.0080.

Rotatory power:

The following page contains a table of observed and molecular rotations.

Rotatory power of d-Octyl Salicylate (M.W. = 250·2)

Solvent	l	t	c	α_{6807}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Homogeneous	1	18	(D= 1·008)	+23·86	+31·53	+36·65	+57·02	+59·20	+78·21	+90·95	+141·5
Ethyl Alcohol	2	17	5·028	+ 2·69	+ 3·74	+ 4·23	+ 6·21	+67·0	+93·1	+105	+155
Ethyl Alcohol + 1 molecular proportion of NaOEt	1	15	4·999	-	-	- 0·43	-	-	-	-21·5	-
Ethyl Alcohol + 1 molecular proportion of KOEt.	2	15	5.546	- 0·20	- 0·59	- 1·08	- 6·14	- 4·5	-13·3	-24·4	-139

d-sec-β-Octyl p-Hydroxybenzoate.

The preparation of this compound was attempted by the same method as was used for the previous compounds, but only a mixture of methyl ester and the free p-hydroxy-benzoic acid was obtained in place of the expected octyl ester. It was thought possible that the phenolic hydroxyl group in the p-position might have a greater effect in precipitating the sodium from solution than was the case with the ortho compound. The preparation was therefore attempted with a greater proportion of sodium, but this was also unsuccessful. Direct esterification by heating the acid and alcohol under reflux with sulphuric acid as catalyst was next tried but no yield of octyl ester was obtained. The acid chloride method used for the corresponding methyl ester by Rule and MacGillivray (J.C.S., 1929,401) was also tried without success. These authors observed that the yield of the menthyl ester was very low and the product impure.

d-sec-β-Octyl m-Hydroxy Benzoate.

The preparation of this compound was attempted, without success, by the sodium catalytic method used for the previous compounds.

Owing to the difficulty of preparation and the/

the losses of octyl alcohol in the attempted methods it was found necessary to abandon the idea of examining these compounds. (Compare also Rule and MacGillivray loc.cit.).

ℓ-Menthyl Quinaldinate.

Quinaldinyl chloride:

18 gm. of quinaldinic acid (Eastman Kodak Co.) were heated with 60 gm. of thionyl chloride under reflux at 60°C for 5 hours. As the mixture darkened considerably, the excess of thionyl chloride was removed from the crystalline acid chloride by filtration. Most of the colouring matter remained in the filtrate. The yellowish solid obtained was again dissolved in thionyl chloride, precipitated by means of benzene, filtered at the pump and dried in a vacuum desiccator. Yield 12 gm. Melting point 175 - 7°C.

ℓ-Menthyl Quinaldinate:

Considerable difficulty was found in converting the acid chloride into the menthyl ester the acid chloride seeming to be comparatively inactive towards menthol. The yield from the above preparation was heated with 12 gm. of menthol under reflux at a temperature of 150 - 170°C. The mixture became brown in colour and hydrogen chloride was evolved, such evolution however being very slow. The heating was stopped after 11 hours as no more hydrogen chloride was being evolved. The mixture was extracted twice with petrol ether. The extracts were combined, evaporated to half bulk, and cooled in ice, when a colourless crystalline solid separated out. The crystals/

crystals were a mixture of two types, needle shaped and cubical. Both had the same melting point and rotation in alcoholic solution. The ester was comparatively insoluble in alcohol. Yield 5 gm. Melting point, 141 - 2°C.

A number of variations were made in the hope of increasing the yield but the above was the best obtained. Menthol appears to react very slowly with this acid chloride.

Analysis:

0.1920 gm. ester gave 0.1452 gm. water and 0.5412 gm. carbon dioxide.

Found C = 76.88% and H = 8.40%

$C_{20}H_{25}O_2N$ requires C 77.1% and H = 8.1%

Rotatory power:

The following page contains the rotations observed under the conditions indicated and the molecular rotations calculated from them.

Rotatory power of l-Menthyl Quinaldinate (M.W. = 311·2)

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	2	16·5	0·9856	-1·15	-1·37	-1·59	-2·65	-182	-216	-251	-419
Ethyl Alcohol + 4 molecular proportions of HCl	2	17·5	0·8696	-1·07	-1·41	-1·61	-3·02	-192	-252	-288	-540

Owing to the slight solubility of this ester in alcohol it was found impossible to obtain a solution of greater concentration than 1%. In order to make the effect due to hydrochloric acid more pronounced at this low concentration four molecular proportions of the acid were used.

d-sec-β-Octyl Quinaldinate.

Quinaldinyl chloride.

After completing the previous preparation a paper was read (by Hammick and Dickinson, J.C.S., 1929, 214) describing a method whereby the acid chloride may be obtained as a low melting solid (m.p. 97°C) in place of the high melting form previously obtained. It was thought possible that this form might be more soluble than the high melting product and thus more readily enter into reaction. Following the directions of the above authors 12 gm. of quinaldinic acid were recrystallised from ligroin (100 - 120°). The 10 gm. of acid so obtained were suspended in 250 c.c. ligroin (100 - 120°), 10.5 gm. of phosphorus pentachloride were added and the mixture was boiled under reflux for three hours, at the end of which time evolution of hydrogen chloride had ceased. The liquid was decanted from a black mass and allowed to cool. The crystals of acid chloride were filtered at the pump. Yield 5 gm.

Methyl Quinaldinate.

Following a method described by Besthorn and Ibele (Berichte, 1906, 39, 2332) the acid chloride was covered with methyl alcohol in which it went completely into solution with slight evolution of heat. The solution was boiled under reflux for two hours after which/

which the methyl alcohol was evaporated off. The residue was dissolved in a small quantity of water and mixed with ether in a separating funnel. Excess of solid potassium bicarbonate was added in small quantities to free the methyl ester from combined hydrogen chloride. Carbon dioxide was evolved and the free ester was taken up by the ether. The ether layer was separated from the water and dried over anhydrous sodium sulphate. On removing the ether and cooling the residual liquid it solidified.

Yield 4½ gm.

Octyl quinaldinate.

This compound was prepared by the sodium method using the solid methyl ester obtained above. The yield in this case was not good, only 1½ gm. of the crude liquid ester were obtained. No further supplies of quinaldinic acid were available and the ester was therefore examined in the unpurified state in order to determine the direction of the change of rotatory power on ionisation.

Analysis: (Ter Meulen's hydrogenation)

0.0504 gm. ester required 3.06 c.c. of .0574 N hydrochloric acid to neutralise the ammonia it produced.

Found N = 4.88%

$C_{18}H_{23}O_2N$ requires N = 4.91%.

Rotatory power:

The following page contains a table of observed and molecular rotations.

Rotatory power of d-Octyl Quinaldinate (M.W. = 285.2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	17	3.808	+1.09	+1.50	+1.86	+3.38	+81.6	+112	+139	+253
Ethyl Alcohol + 1 molecular proportion of HCl	1	18	3.370	+0.90	+1.17	+1.34	+2.74	+76.2	+99.0	+113	+232

l-Menthyl Picolinate.

Picolinyl chloride.

The acid chloride was prepared in the same way as the high melting quinaldinyl chloride, using 15 gm. of picolinic acid (Eastman Kodak, Co.). In place of filtering off excess thionyl chloride, it was removed by heating under diminished pressure.

Methyl Picolinate:

This compound was prepared by the same method as the corresponding quinaldinate, The fraction boiling at 120 - 140°C (chiefly 140°) under 10 mm. pressure was retained. This was a white crystalline solid melting at 14°C (Engler, Ber.,1894,27,1785, quotes 14°). Yield 4½ gm.

l-Menthyl Picolinate, was prepared by the sodium method, the quantities used being 0.1 gm. sodium, 4½ gm. methyl picolinate and 6½ gm. menthol. The mixture was heated under diminished pressure in order to remove unchanged menthol (b.p. 100 under 10 mm.) and methyl picolinate (b.p. 140 under 10 mm.). The residue was dissolved in ether and dried over anhydrous sodium sulphate. The solution was evaporated to small bulk and the residual ether removed in a hot vacuum desiccator, when a brown viscous liquid remained. After determining the rotatory power of this product in ethyl alcohol solution the liquid was distilled/

distilled under diminished pressure and the fraction boiling at 170° C under 1 mm. was retained. The distillate was colourless and odourless but remained a viscous liquid, and had the same rotatory power in ethyl alcohol solution as before. Yield 5 gm.

Analysis (by Dumas's method)

0.1847 gm. ester gave 8.5 c.c. Nitrogen at 15.5°C and 755.5 mm. pressure.

Found N = 5.41%

$C_{16}H_{23}O_2N$ requires N = 5.36%

Rotatory power:

The following page contains a table of observed and molecular rotations.

Rotatory power of *l*-Menthyl Picolinate (M.W. = 261.2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	17	4.368	-2.70	-3.33	-3.94	-6.67	-162	-199	-236	-399
Ethyl Alcohol + 1 molecular proportion of HCl	1	18	4.363	-2.53	-3.21	-3.76	-6.27	-152	-192	-225	-376

d-sec-β-Octyl Picolinate.

This compound was prepared in the same manner as the corresponding menthyl ester. 15 gm. of the acid were used and from this only 5½ gm. of the methyl ester were obtained. The octyl ester boiled at 170 - 173° under 12 mm. Yield 5 gm. Two fractionations were necessary to obtain a product having a constant rotation in the homogeneous state. The ester was a slightly yellowish liquid.

Analysis: (by Ter Meulen's hydrogenation)

.0797 gm. of ester required 5.72 c.c. of .0574 N hydrochloric acid to neutralise the ammonia it produced.

Found N = 5.77%

$C_{14}H_{21}O_2N$ requires N = 5.95%

Rotatory power:

The succeeding page contains a table of observed and molecular rotations.

Rotatory power of d-Octyl Picolinate (M.W. = 235.2).

Solvent	l	t	c	α_{6708}	α_{5893}	α_{5461}	α_{4358}	$[M]_{6708}$	$[M]_{5893}$	$[M]_{5461}$	$[M]_{4358}$
Ethyl Alcohol	1	16	5.240	+1.56	+1.99	+2.38	+4.26	+70.0	+89.3	+107	+191
Ethyl Alcohol + 1 molecular proportion of HCl	1	17.5	6.810	+1.81	+2.34	+2.81	+5.11	+62.5	+80.8	+97.0	+176

DISCUSSION.

Value of the Sodium Alkoxide Catalytic Method for the Preparation of Higher Esters.

The sodium catalytic method used for preparing the majority of the esters dealt with in this thesis has already been described in detail. Good results were obtained with the amino and dimethylamino esters, except the m-amino compound which gave only a 10% yield, whereas the others gave yields ranging from 20 to 50%. The low yield of the m-amino ester does not seem to be due to failure of the method of preparation but to decomposition during subsequent distillation, the ester appearing to be unstable at high temperatures. The preparation of the hydroxy esters was not so successful by this method, octyl salicylate (39% yield) being the only one obtained. This is probably due to the low solubility of the sodio-derivatives of the m- and p-hydroxy esters in octyl alcohol.

It is well known that amino- and hydroxybenzoic esters of a secondary alcohol such as menthol are not prepared without considerable difficulty. Cohen (J.C.S.,1914,105,1892) prepared the o-,m-, and p-dimethylaminobenzoic esters of menthol by the acid chloride/

chloride method, and isolated them as viscous, highly coloured liquids. Rule and MacGillivray (J.C.S., 1929, 401) repeated the preparation of the ortho derivative and showed that Cohen's product was far from pure. The latter authors failed to obtain the m- and p-isomerides by this method, nor were they able to convert the o-, m-, and p-aminobenzoic acids into the menthyl esters, either directly or by way of the acid chloride. The amino esters were finally obtained from the corresponding nitro-esters (in 100, 40 and 10% yields respectively, calculated from the nitro-compounds). Using the sodium alkoxide method these esters may be rapidly prepared in the optically pure state in yields varying from 10% (m-amino ester) to 40% (p-dimethylamino ester) calculated on the methyl esters. In each case the excess of optically active octyl alcohol was recovered.

As stated above octyl salicylate was obtained in 39% yield by the alkoxide method. Rule and MacGillivray (loc.cit.) were unable to isolate the pure menthyl m- and p-hydroxybenzoic esters and in these cases the alkoxide method also failed.

The methyl esters required for the alkoxide process were readily obtained. In several cases they were standard chemicals and in others were prepared from the acid by simple esterification. The methyl esters/

esters of picolinic and quinaldinic acids proved more difficult to obtain in quantity, but by using the sodium alkoxide method they were converted into the menthyl and octyl esters in 8 - 10 days starting from the acids. On the other hand, the preparation of menthyl quinaldinate by direct esterification of the acid chloride required a somewhat longer period. This is due partly to the time involved in isolating the pure acid chloride and partly to the slowness with which the acid chloride reacts with the secondary alcohols employed.

In the picolinic series the yields from the sodium catalytic method were in the neighbourhood of 20% of the theoretical (calc.on acid). The yields of methyl ester were approxi_mately 30% of the theoretical and the yields of menthyl or octyl ester from this were 50 -60% of the theoretical. The yield of menthyl quinaldinate obtained by direct esterification of the acid chloride was only 12% of the theoretical as calculated from the am_ount of acid employed.

The purification of the sec-β-octyl esters was found to be an easy matter. It was only necessary to extract the mixture with ether, wash with dilute acid or alkali and with water, dry over a suitable drying agent and distil. The esters were thus obtained in such purity that only one or at most two/

two additional fractionations were necessary to obtain them in a state of optical purity.

It was thought that under the conditions of experiment the strong alkali present might have an adverse effect on the optical activity of the menthol or octyl alcohol. To determine whether or not this was the case one of the octyl esters, octyl anthranilate, was hydrolysed and the rotatory power of the sample of octyl alcohol obtained from it was measured. The rotatory power of the octyl alcohol had changed from $\alpha_D^{16} = 8.12$ to $\alpha_D^{16} = 8.08$. As the amount of octyl anthranilate available for hydrolysis was rather small, the quantity of octyl alcohol obtained from it was probably insufficient for thorough fractionation. It is evident, however, that little or no racemisation had taken place. After the completion of the above part of this thesis, Dr J.Spence prepared *l*-menthyl 3-hydroxy-2-naphthoate (to be published shortly by Rule and Spence) by the sodium catalytic method. Having already prepared this compound by another method, he found, on comparing the two samples, that their rotatory powers were identical. *l*-Menthyl o-dimethyl-amino benzoate prepared by C.F.Campbell using the sodium method was found to have the same rotation as this compound prepared by way of the acid chloride. (Rule and MacGillivray, J.C.S., 1929, 407). It may

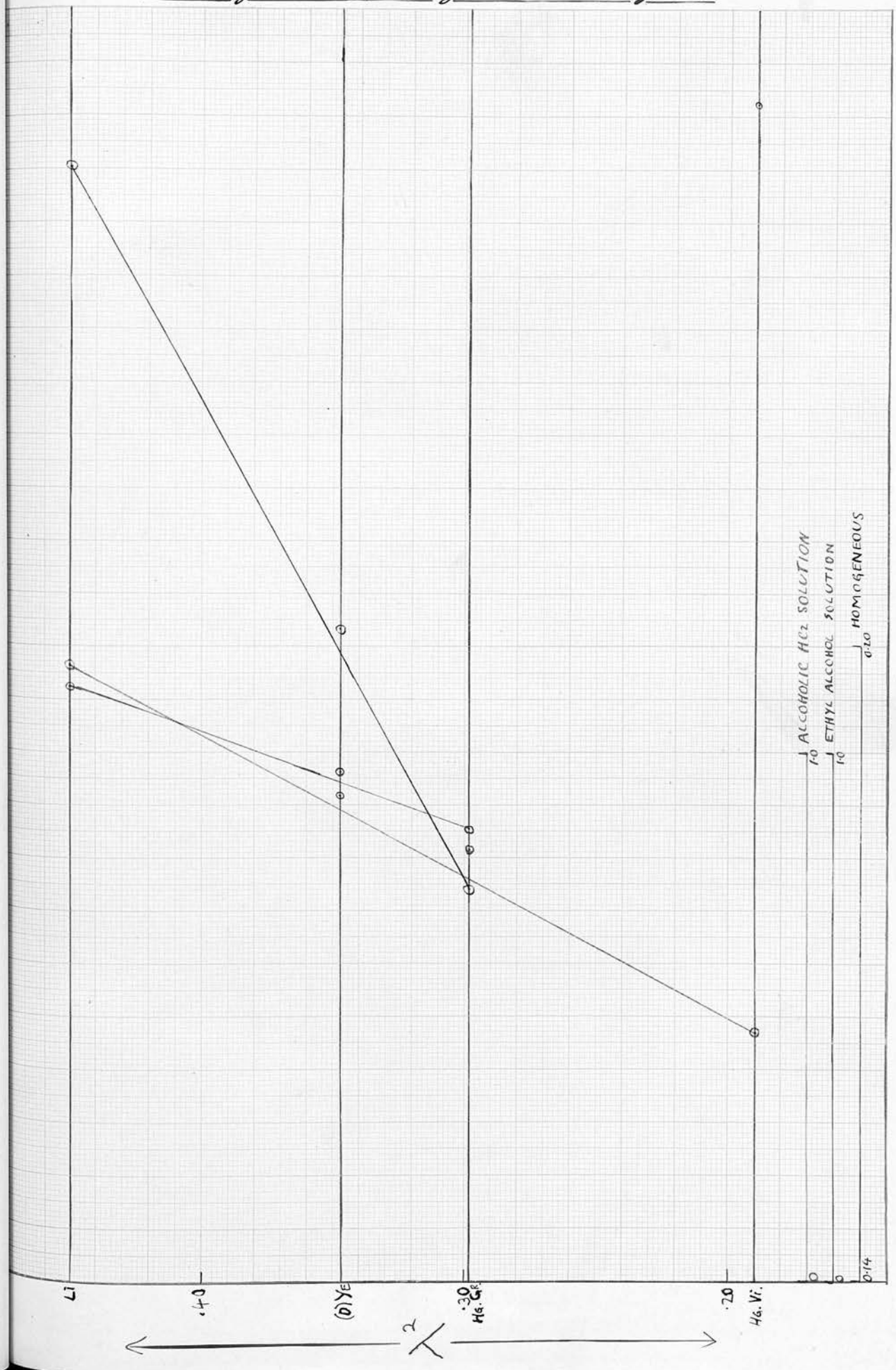
therefore be concluded that the use of sodium does not lead to any appreciable racemisation in these cases. This is in agreement with the experiments of Pickard and Kenyon on the action of alkalis on esters of optically active secondary alcohols (J.C.S., 1911, 99, 62).

In conclusion, it may be said that the sodium catalytic method of preparing the above menthyl and octyl esters has the advantage over previous methods in the rapidity with which it can be carried out and in the yields obtained. This applies particularly to the esters of certain amino- and hydroxybenzoic acids which are difficult to obtain by the more usual methods. The optical purity of the esters can also be compared favourably with that obtained by other methods. The process should prove a decided benefit to workers in this branch of chemistry both in the above respects and in its possible application to other compounds which cannot be prepared at all by the ordinary methods involving the use of acid media.

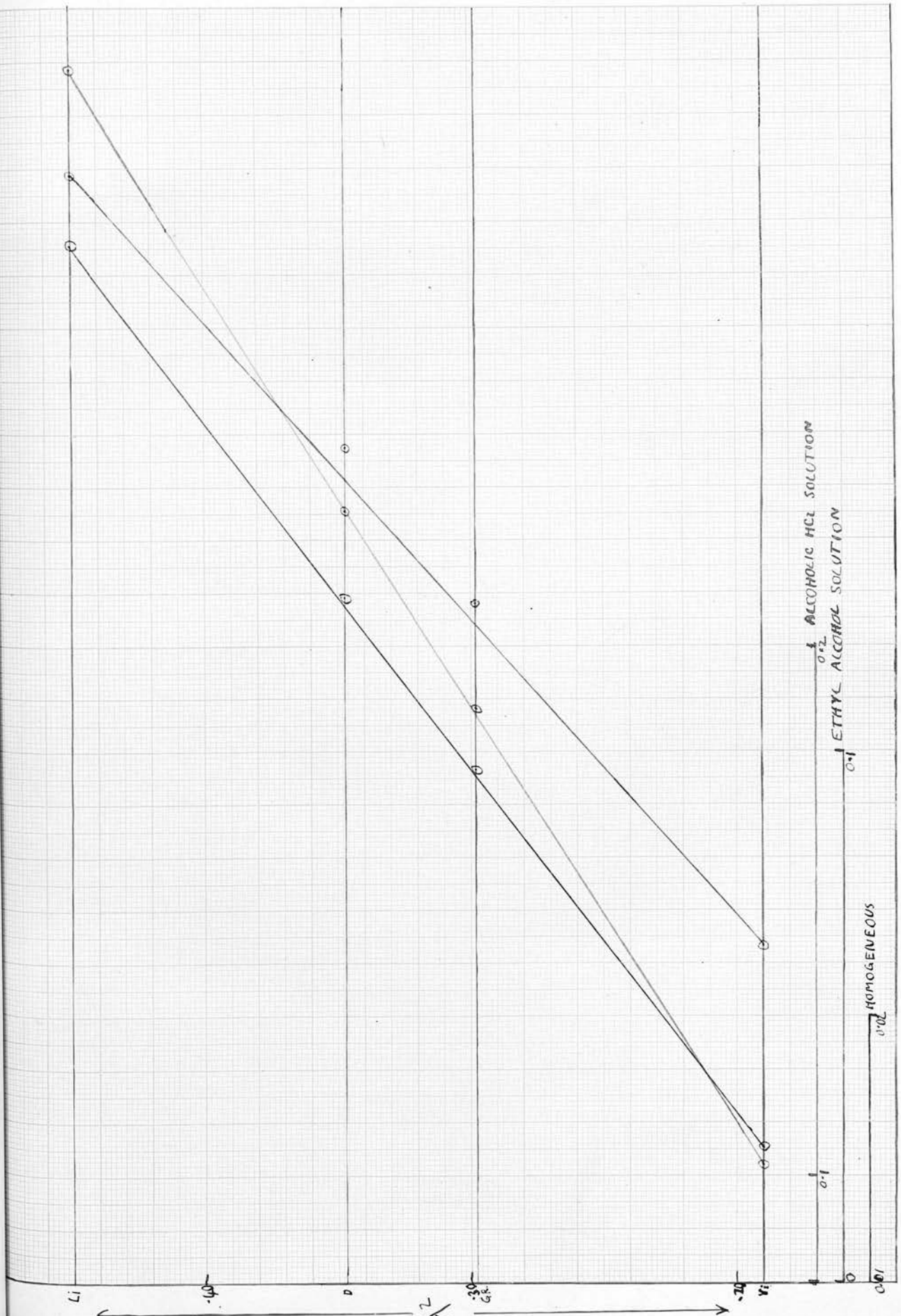
DISPERSION.

In dealing with this aspect of the esters examined in this thesis it is necessary to refer to the graphs of λ^2 against $1/\alpha$ for the different compounds in the various solvents employed. These graphs will be found on the following pages.

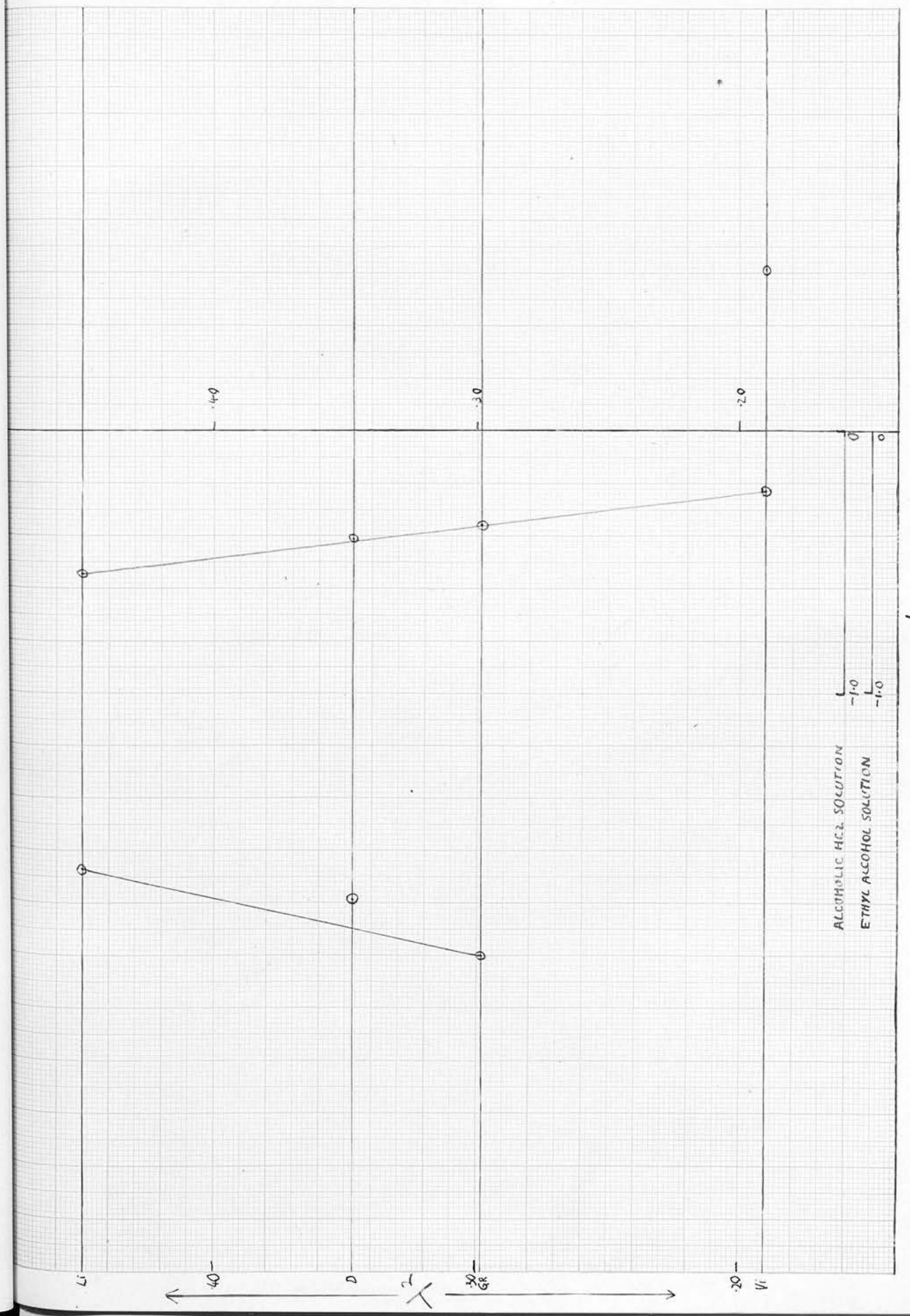
d-Octyl o-Dimethylamino-benzoate

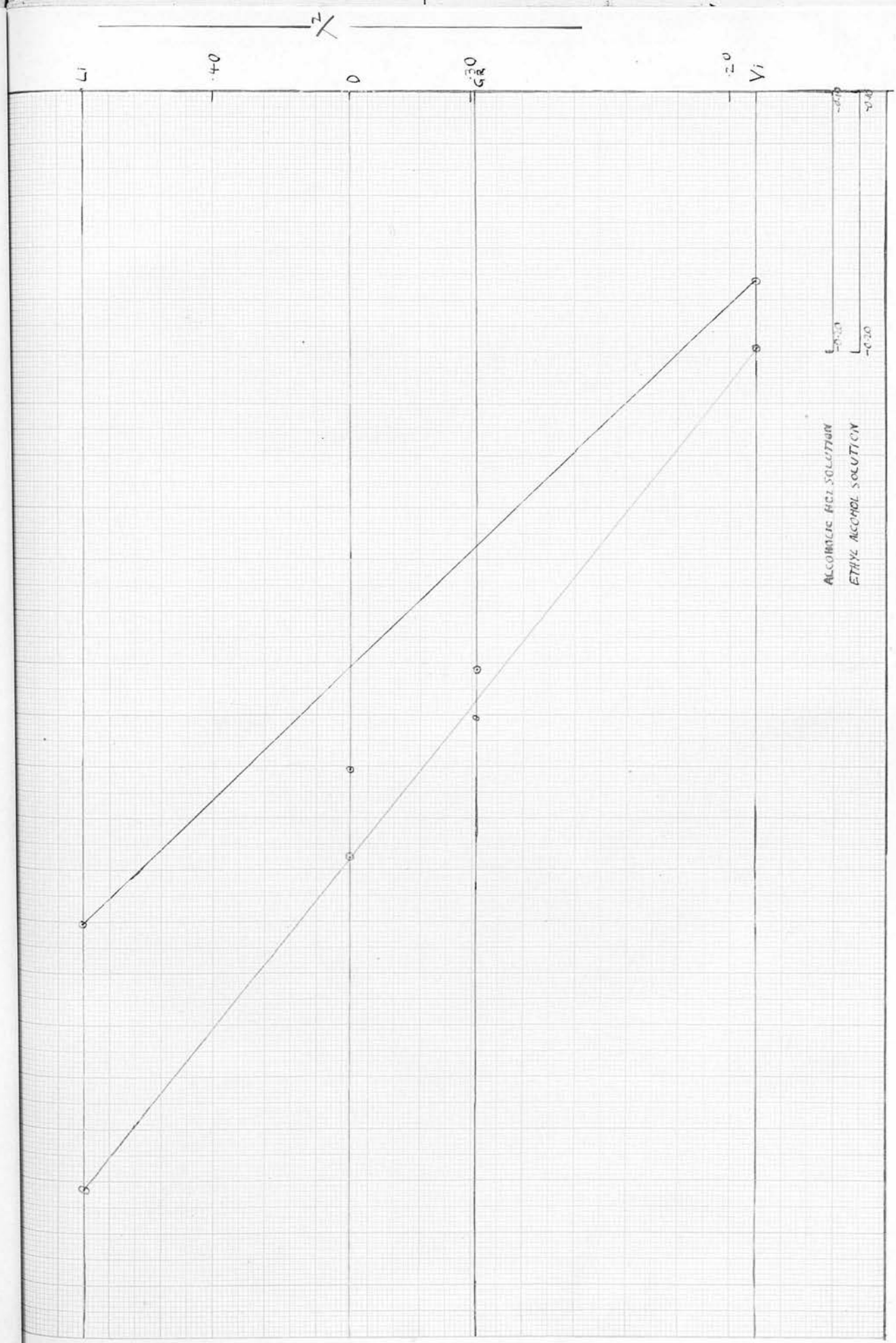


d-Octyl p-Dimethylamino-benzoate

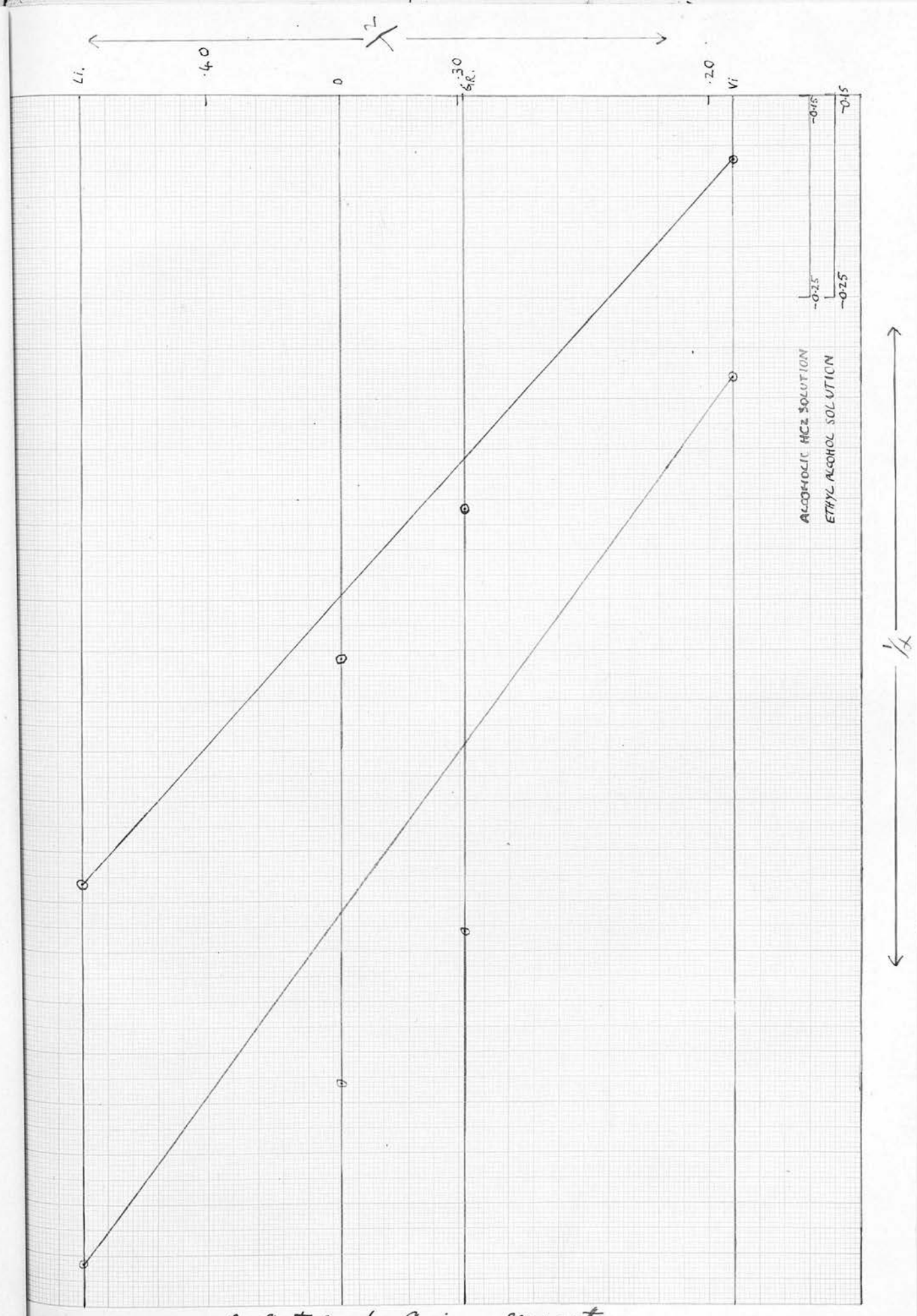


l - Octyl Anthranilate

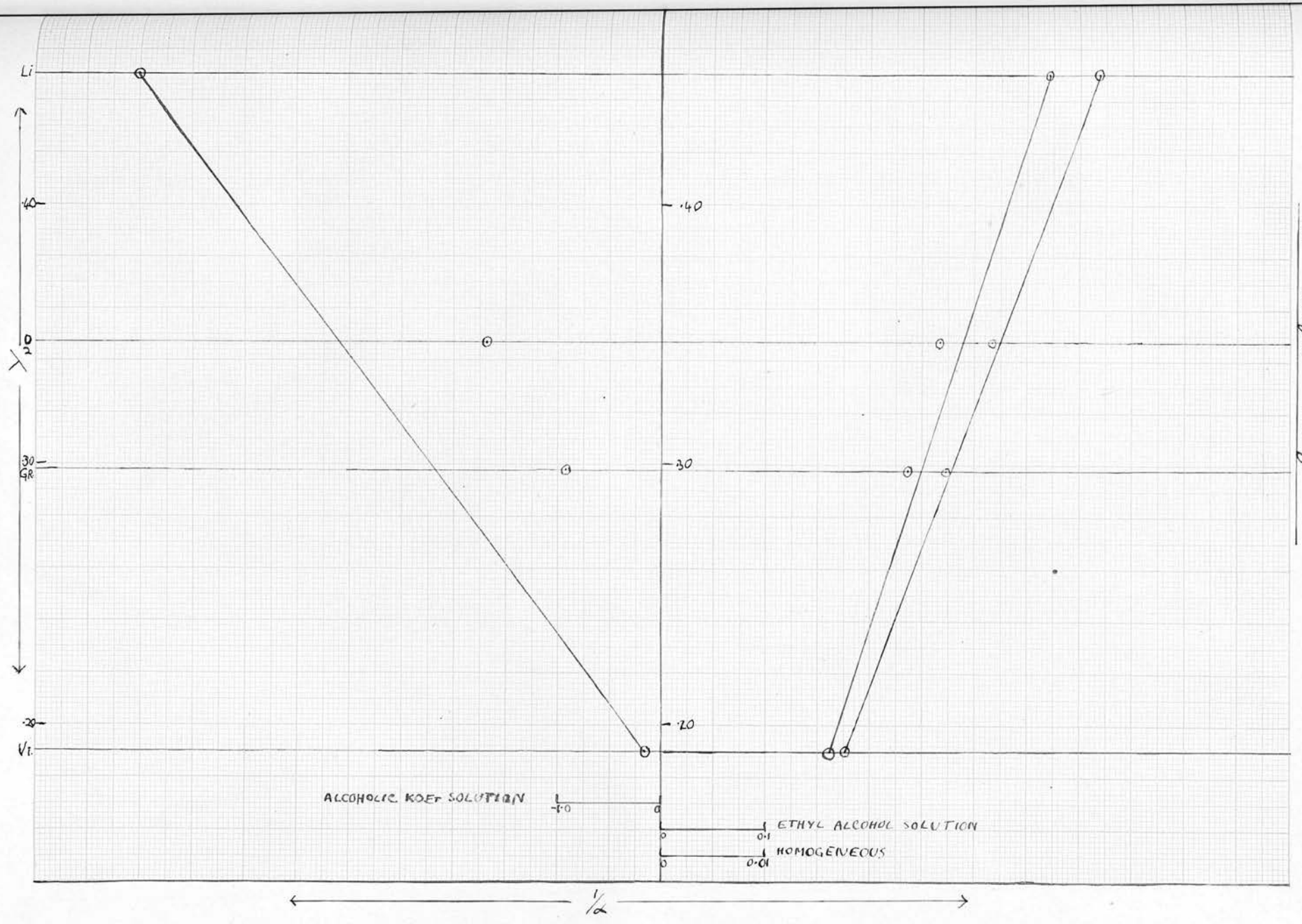




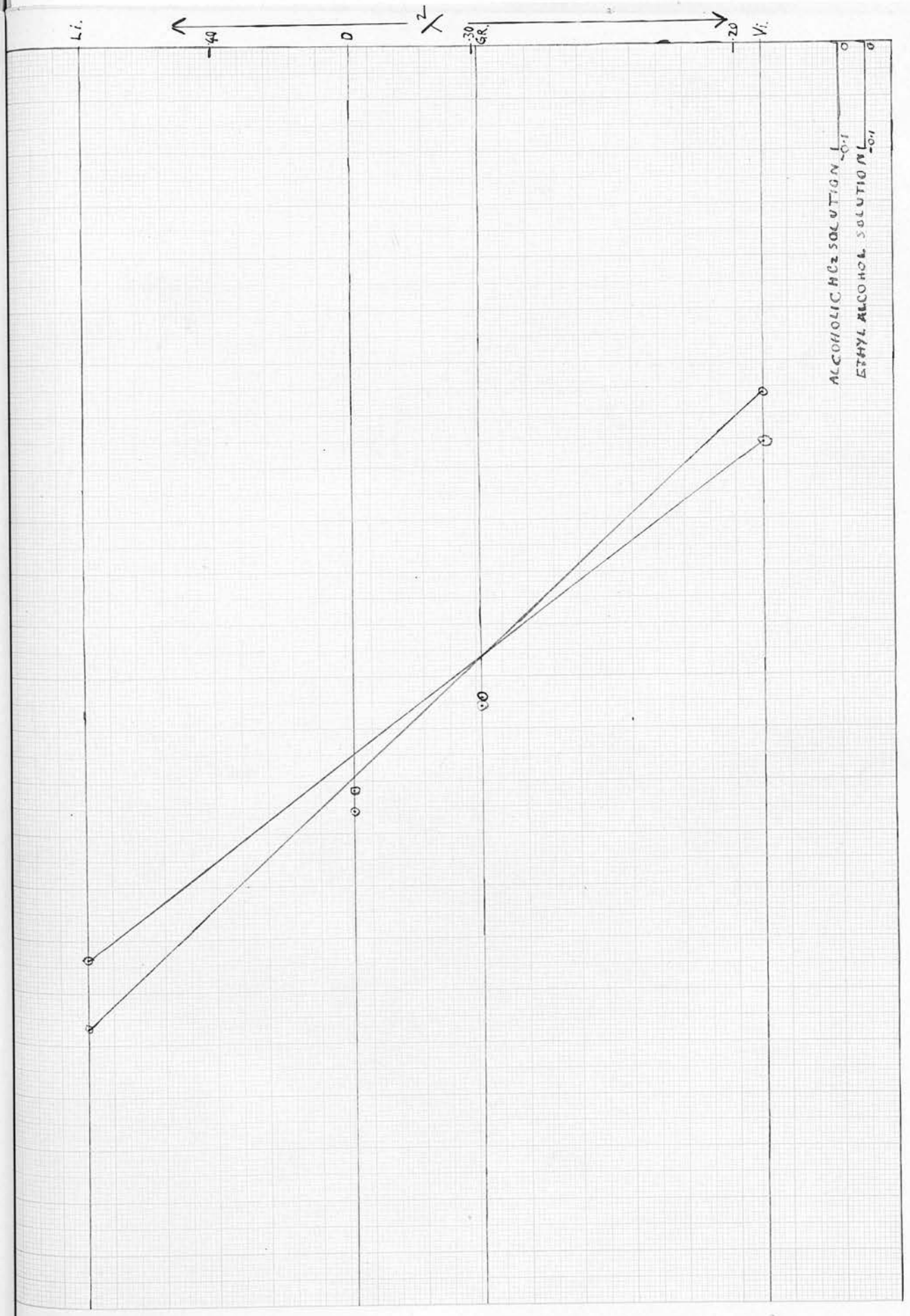
l - Octyl m - Amino - benzoate



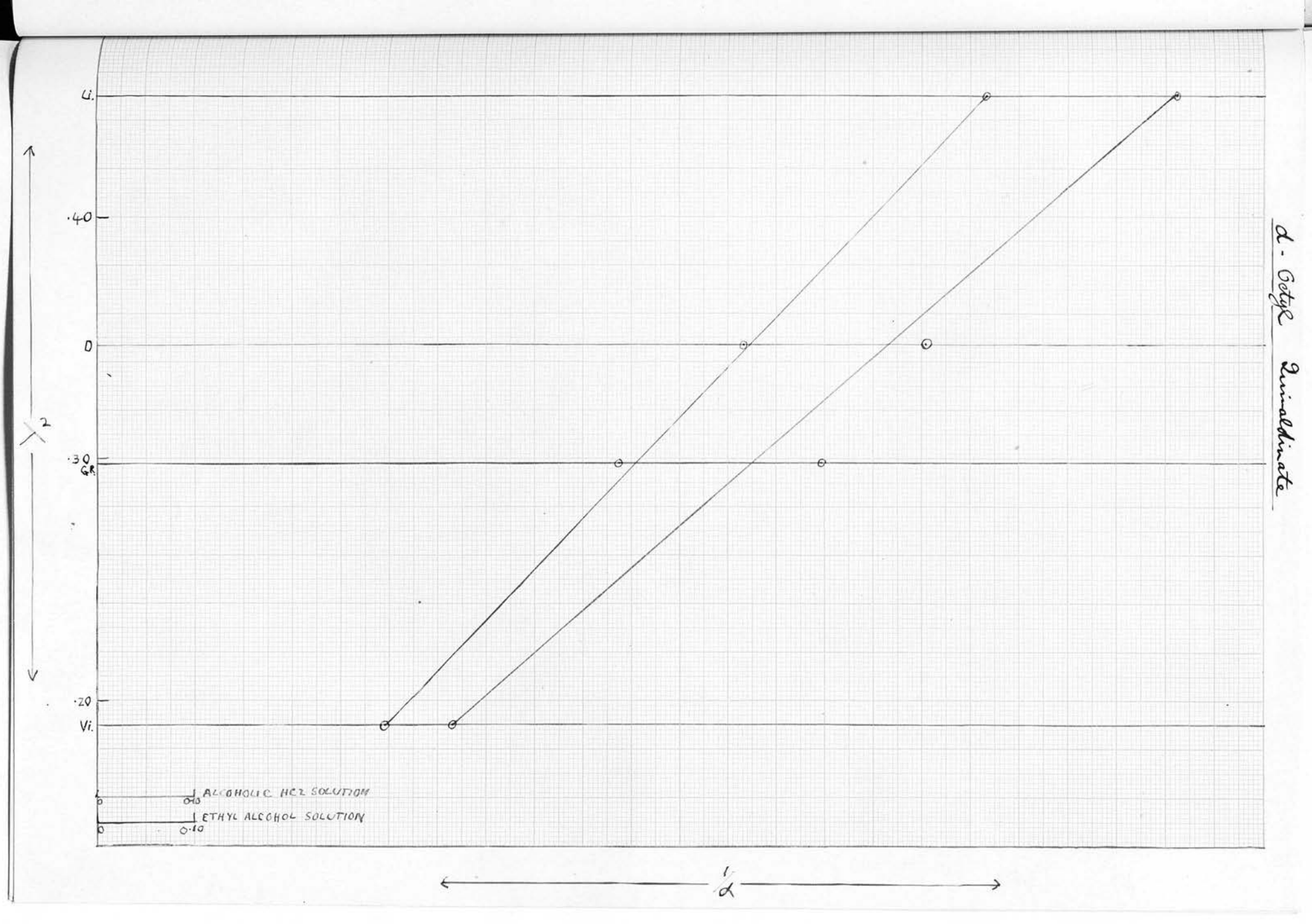
l-Octyl p-Amino-benzoate

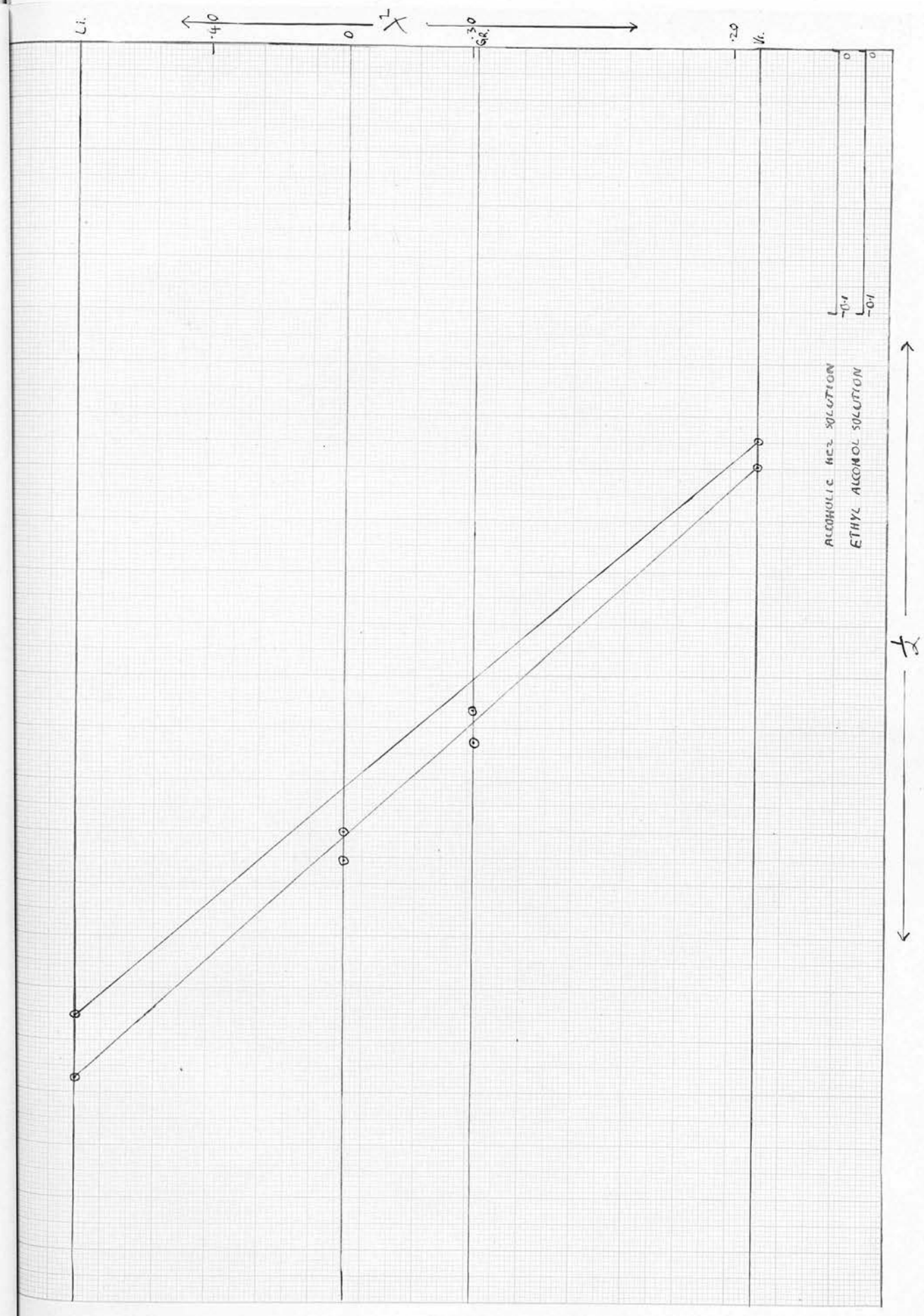


α - Betyl Salicylate



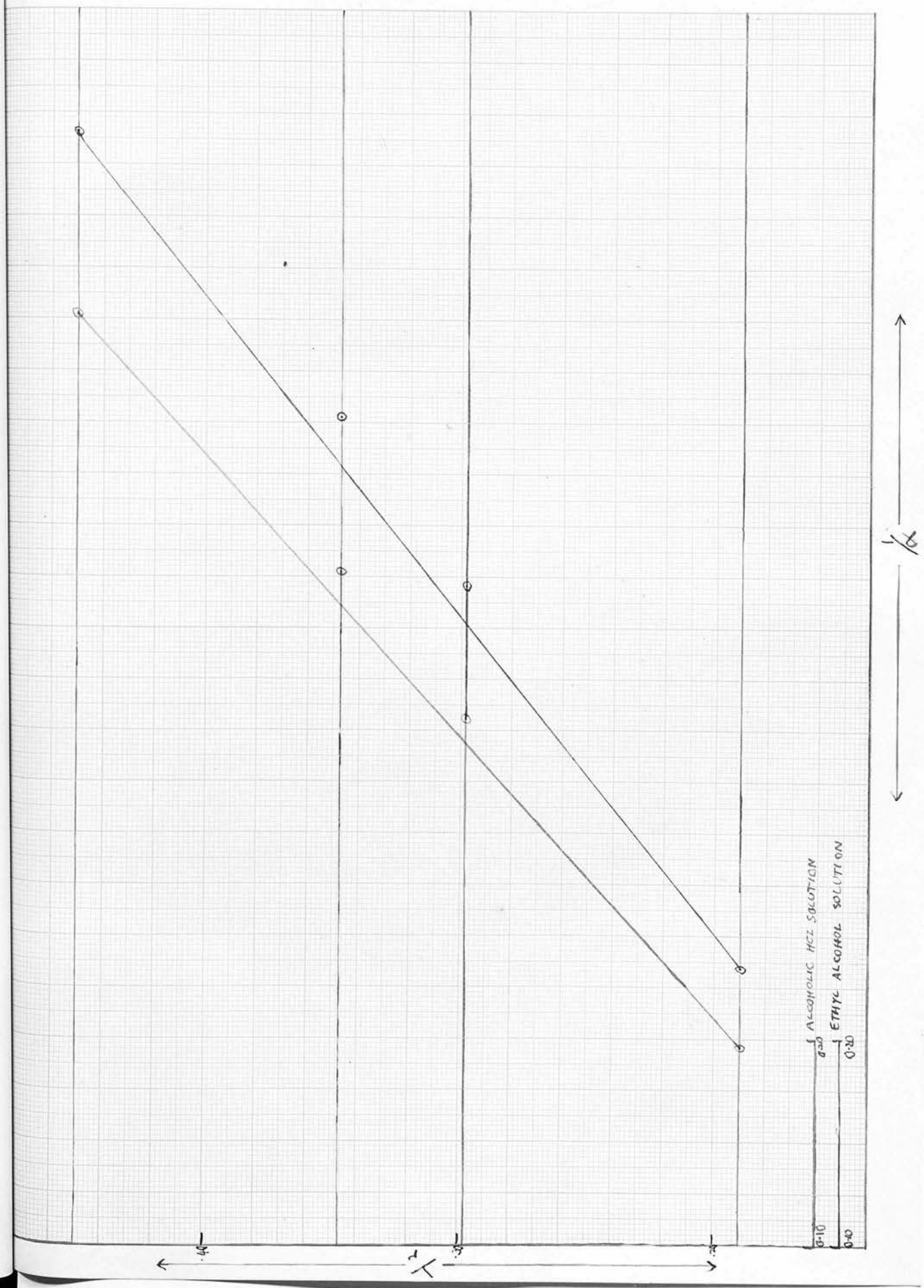
l - Menthyl Quinaldinate


d - Getyk Quinaldinate
Li.
·40
0
·30
GR.
·20
Vi.
1/d
ALCOHOLIC HCl SOLUTION
0·0
ETHYL ALCOHOL SOLUTION
0·0
0·10



l - Menthyl Picolinate

d - Cetyl Picolinate



As is evident from the graphs, the compounds exhibit complex dispersion. The cases of the octyl o-dimethylamino- and o-amino-benzoates are specially noticeable. In ethyl alcoholic solution both these compounds exhibit anomalous dispersion. The dispersion of the o-dimethylamino-benzoate in methyl alcohol solution is also anomalous and in the homogeneous state the absorption of light in the violet region is so marked that no value of α_{4358} could be obtained.

The l-sec-β-Octyl o-amino-benzoate gives negative values for α_{6708}, α_{5893}, and α_{5461}, and a positive value for α_{4358}. In both cases the dispersion of the esters in alcoholic solution containing a molecular proportion of hydrogen chloride was only slightly complex. The salicylate exhibits slightly complex dispersion in the homogeneous state and in ethyl alcohol solution and highly complex dispersion in ethyl alcohol solution containing a molecular proportion of potassium ethoxide. In no case however, is the dispersion of the salicylate anomalous. Rule and MacGillivray (J.C.S., 1929,401) found that l-menthyl salicylate exhibited complex dispersion in the same solvents.

Values of α_{vi}/α_D

Substance	Solvent	T	α_{vi}/α_D
Octyl o-Dimethyl-Aminobenzoate	Ethyl Alcohol	16°C	0.413
	Ethyl Alcohol + 1 mol.prop.HCl	15	2.06
Octyl p-Dimethyl Aminobenzoate	Homogeneous	16	2.38
	Ethyl Alcohol	17	2.48
	Ethyl Alcohol + 1 mol.prop.HCl	16	2.21
Octyl Salicylate	Homogeneous	18	1.81
	Ethyl Alcohol	17	1.66
	Ethyl Alcohol + 1 mol.prop.KOEt.	15	10.42
Octyl Anthranilate	Ethyl Alcohol	17.5	-
	Ethyl Alcohol + 1 mol. prop.HCl	14.5	1.79
Octyl m-Amino-benzoate.	Ethyl Alcohol	17.5	2.09
	Ethyl Alcohol + 1 mol.prop.HCl	18.5	1.99
Octyl p-Amino-benzoate	Ethyl Alcohol	17.5	2.37
	Ethyl Alcohol + 1 mol.prop.HCl	14	2.21
Octyl Quinaldinate	Ethyl Alcohol	17	2.25
	Ethyl Alcohol + 1 mol.prop.HCl	18	2.34

Values of α_{vi}/α_D (continued)

Substances	Solvent	T	α_{vi}/α_D
Octyl Picolinate	Ethyl Alcohol	16°	2.14
	Ethyl Alcohol + 1 mol.prop.HCl	17.5	2.18
Menthyl Quinaldinate	Ethyl Alcohol	16.5	1.93
	Ethyl Alcohol + 4 mol.prop.HCl	17.5	2.14
Menthyl Picolinate	Ethyl Alcohol	17	2.00
	Ethyl Alcohol + 1 mol.prop.HCl	18	1.95

As was to be expected, abnormal values of α_{vi}/α_D are observed for the octyl salicylate in ethyl alcohol solution containing potassium ethoxide and for the o-amino and o-dimethylamino esters in ethyl alcohol. All these esters exhibit anomalous or very complex dispersion.

Rotatory Powers of Non-ionised Esters.

As has already been stated in the introduction (p. 6) it has been concluded from the examination of a large number of *l*-menthyl esters of substituted benzoic acids, that a definite regularity exists among the ortho compounds. It has been found that an o,p-directive substituent depresses and a m-directive group raises the rotatory power as compared with the unsubstituted benzoate. The only known exceptions are the menthyl esters of salicylic and anthranilic acids, the abnormally high rotatory powers of which were explained by Rule and MacGillivray (J.C.S.,1929,401) as being due to chelation of the hydroxy or amino group with the carboxylic keto group.

Octyl benzoates which have non-ionisable substituents (Rule,Hay,Numbers and Paterson,J.C.S., 1928,178 see introduction p.11) also exhibit the same regularity, the order of the substituents being approximately the same as that found for the menthyl esters.

For purposes of comparison the values of $[M]_{5461}$ at room temperatures for the known *l*-menthyl and octyl esters of o-substituted benzoic acids (including those described in this thesis) are summarised/

summarised in the following table.

Ortho-Substituted Benzoic Esters (Homog.or in alcohol)

Substituent	1-Menthyl $[M]_D$	1-Octyl $[M]_D$	1-Octyl $[M]_{5461}$ *
NO_2	-381°	-122°	-151°
COOH	332	117(alc)	163(alc)
H	239	78	111(alc)
OH	279	93.1(alc)	105(alc)
CH_3	231	68.1	80.9
I	237	44.3	53.2
Br	205	49.2	58.6
Cl	195	47.1	55.9
OMe	148	33.0	37.6
NMe_2	200	29.6(alc)	31.7
NH_2	261(alc)	23 (alc)	21

(Many of these values are taken from the table given in J.C.S., 1928,180).

* On account of their greater accuracy, rotatory powers for the mercury green line, λ_{5461}, are used when available throughout this thesis.

Reference to the above table shows that the general regularities noted by Rule,Hay,Numbers and Paterson also hold for the amino,dimethylamino and salicylic esters. Octyl salicylate, however, does not have a rotation corresponding to that of the menthyl ester, for which the value is abnormally high, but has a value slightly lower than that of the unsubstituted/

unsubstituted benzoate. Considerable chelation probably exists even in the octyl ester, as the rotation is higher than would have been expected from the strong o,p-directive influence of the hydroxyl group. Octyl anthranilate has a much lower rotation whereas the corresponding menthyl compound has a higher value than the unsubstituted ester.

Sidgwick in "The Electronic theory of Valency p.117" states that hydrogen attached to nitrogen (forming an NH_2 group) coordinates much less easily than when attached to oxygen in an OH group. The above rotations for octyl salicylate and anthranilate are in agreement with this statement and for the menthyl esters also the salicylate has a higher value than the anthranilate. The octyl o-dimethylamino-benzoate has a much lower rotation than the unsubstituted ester. The o,p-directive substituents OH, NH_2 and NMe_2 therefore lead in every case to a lowering of the rotatory power when present in the ortho position in octyl benzoate.

p-Substituted Esters

Substit.	ℓ-Menthyl $[M]_D$	ℓ-octyl $[M]_D$	ℓ-octyl $[M]_{5461}$ (homog.or in alcohol)
H	-239°	-78°	-111° (alc.)
CH_3	246	103	123
Cl	237	104	124
OCH_3	250	113	136
COOH	259	119	145 (alc.)
NO_2	235	120	145
NH_2	224(alc.)	134	163 (alc.)
NMe_2	-	174	213 (alc.)

The NH_2 of NMe_2 group introduced in the para position in octyl benzoate produced an unusually great increase in rotatory power compared with the effect of groups such as Cl, NO_2, COOH or OMe. The boiling points of these para substituted basic esters also indicate that there is some thing unusual in these compounds. As shown by the following figures an O-NMe_2 group produced a pronounced lowering of boiling point and a p-NMe_2 or p-NH_2 group an unusual increase.

Substituent	O-NH_2	p-NH_2
B.p. of octyl benzoates.	183°/10 mm.	200°/8 mm.
" " "	o-NMe_2 126°/ 0.2 mm.	p-NMe_2 180°/1.8 mm.
" " "	o-OMe 187°/ 13 mm.	p-OMe 189°/ 13 mm.

The/

The boiling points of the o- and p-methoxy esters (Rule and Numbers, J.C.S., 1926, 2121) are included in the above table to illustrate a normal case. The reduction of pressure from 10 - 12 mm. to the low pressure given by a Gaede pump (approximately 0.2 - 1 mm. in the above cases) usually results in lowering the boiling points of esters of this type by from 40 - 60°. The above figures indicate, therefore, that the p-dimethylamino ester and, to a lesser extent the p-amino ester have exceptionally high boiling points. The boiling points of these para esters are in agreement with Sidgwick's conclusions on the abnormal properties of isomeric benzene derivatives containing an NMe_2 or NH_2 group and an ester grouping (Sidgwick, J.C.S., 1920, 392).

The high rotatory powers and high boiling points of the unionised para substituted basic esters might have been due therefore, to some kind of molecular association.

This point was tested by determining the molecular weight of the p-dimethylamino ester in benzene by the freezing point method. The values found were 272 and 276, as compared with the formula weight 277.

The carboxyl derivatives were not examined, as MacGillivray (thesis submitted in May 1928) had already examined them. The relative position of these carboxyl derivatives can be seen from the following table/

table, in which HCl, NaOEt or KOEt indicates the presence of 1 molecular proportion of these reagents.

Ionised Esters.

Ester	Solvent	$[M]_{5461}$
Menthyl o-dimethylaminobenzoate	Ethyl Alcohol	-250°
	Alcoholic HCl	-292
Octyl o-dimethylaminobenzoate	Ethyl Alcohol	-31.7
	Alcoholic HCl	-68.5
Octyl p-dimethylaminobenzoate	Ethyl Alcohol	-213
	Alcoholic HCl	-147
Menthyl Anthranilate	Ethyl Alcohol	-313
	Alcoholic HCl	-290
Menthyl m-aminobenzoate	Ethyl Alcohol	-281
	Alcoholic HCl	-271
Menthyl p-aminobenzoate	Ethyl Alcohol	-259
	Alcoholic HCl	-262
Octyl Anthranilate	Ethyl Alcohol	-20.7
	Alcoholic HCl	-63.7
Octyl m-aminobenzoate	Ethyl Alcohol	-121
	Alcoholic HCl	-119
Octyl p-aminobenzoate	Ethyl Alcohol	-163
	Alcoholic HCl	-109
Menthyl Salicylate	Ethyl Alcohol	-299
	Alcoholic KOEt	-246
d-Octyl Salicylate	Ethyl Alcohol	105
	Alcoholic KOEt	-24.4
	Alcoholic NaOEt	-21.5
Octyl hydrogen phthalate	Ethyl Alcohol	-163
Sodium salt	Ethyl Alcohol	-83.4
Octyl hydrogen terephthalate	Ethyl Alcohol	-145
Sodium salt	Ethyl Alcohol	-148
Menthyl hydrogen phthalate	Ethyl Alcohol	-346
Sodium salt	Ethyl Alcohol	-261

It will be seen from the above table that the changes in rotatory power produced by ionisation of the ortho substituted esters are in the direction expected from the corresponding changes in the orienting power of the ionised substituent groups. In the amino ester NH_2 is o,p-directive whereas $-\overset{+}{N}H_3$ is m-directive. This is proved by the fact that aniline nitrated with excess of nitric or sulphuric acid present forms a considerable proportion of m-nitraniline. In agreement with this the rotatory power of the anthranilic ester rises considerably on addition of one molecule of hydrochloric acid. There is a similar rise in the case of the o-dimethylamino ester. These octyl esters differ, however, from the corresponding menthyl derivatives in that the rotations do not rise above that of the unsubstituted ester. As was to be expected from the nature of the charge and the powerful o-,p-directive character of $-\bar{O}$ and $-C\bar{O}O$ the effect of ionisation on octyl salicylate is in the opposite direction to the effect on the anthranilate. Ingold (Ann. Rep. Chem. Soc., 1926,133) states that a negative pole represents the most powerful known o,p-directive influence. Since the change in rotatory power in the presence of NaOEt or KOEt is very pronounced, the sign being actually reversed, it probably represents the conversion of any chelated hydroxy ester present into the open type as well as more or less complete ionisation/

ionisation of the hydroxyl group. As can be seen from the table, ionisation of the p-amino and p-dimethyl amino derivatives reduced the abnormally high values to values of the same order as those found for other para substituted esters.

Octyl m-Aminobenzoate lies between the o- and p-isomerides in its behaviour, the rotatory power falling very slightly on ionisation

Basic Esters containing Nitrogen in the Ring.

Ester	Solvent	$[M]_{5461}$
Menthyl Quinaldinate	Ethyl Alcohol	-251°
	Alcoholic HCl	-288
Octyl Quinaldinate	Ethyl Alcohol	-139
	Alcoholic HCl	-113
Menthyl Picolinate	Ethyl Alcohol	-236
	Alcoholic HCl	-225
Octyl Picolinate	Ethyl Alcohol	-107
	Alcoholic HCl	- 97

The rotatory powers of the ester of picolinic and quinaldinic acids show less definite changes on ionisation. The changes in each case are much smaller than those described above for the amino-benzoates. l-Menthyl quinaldinate in alcoholic solution shows an increased rotatory power in the presence of hydrochloric acid and thus resembles the o-amino and o-dimethylamino esters. l-Menthyl picolinate and d-/octyl quinaldinate/

quinaldinate and picolinate each have a somewhat lower rotatory power in the form of their hydrochlorides. The last three compounds therefore resemble octyl m-amino benzoate rather than the o-compound. Except for the menthyl quinaldinate the behaviour of these esters containing nitrogen in the ring is not in agreement with the above regularities unless the effect is considered as being transmitted directly through space.

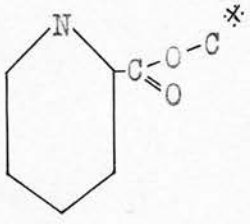
SUMMARY AND CONCLUSION.

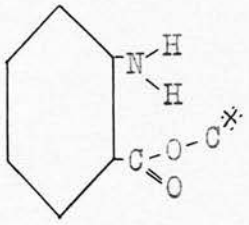
A parallel between the orienting powers of substituents and their influence on the rotatory power of *l*-menthyl and sec-*β*-octyl esters of ortho substituted benzoates has been established by Rule and his co-workers (loc.cit.). This has now been shown to hold for octyl benzoates containing the ionisable substituents OH, NH_2, and NMe_2. As is the case with other o- and p-directive groupings these substituents lower the rotatory power of sec-*β*-octyl benzoate. On ionisation the hydroxyl group becomes more strongly o,p-directive and the rotatory power is so greatly depressed that the sign of the rotation is reversed. The amino and dimethylamino groups, on the other hand, change, on ionisation, from o,p-directive to m-directive groups. In agreement with this, the hydrochlorides of the basic esters have much higher rotatory powers than have the free esters.

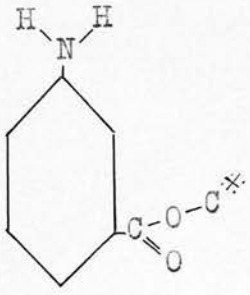
The rotatory powers of the octyl p-substituted amino and dimethylamino benzoates are unexpectedly high, but on ionisation they drop to normally high values of the same order as those of the nitro, carboxy, or methoxy derivatives.

The effect of substituent groupings on the rotatory/

rotatory powers of octyl and menthyl benzoates seems to be propagated through space and not through the chain of atoms. If the effect were transmitted through the chain in a similar manner to the way in which the orienting influences are supposed to be propagated according to Robinson, Ingold, or Flürscheim, it should be evident in other positions in the ring as well as the ortho position. We should therefore expect to find the peculiar o-effect in the para position, but the results obtained confirm those of Rule and MacGillivray in showing that this is not the case. Propagation through space possibly explains also the absence of this influence in the quinaldinic and picolinic esters, in which the nitrogen atom is one degree further removed than in the o-amino esters, and thus resembles the m-compound in so far as space influence is concerned.







※ optically active carbon atom.

The sodium alkoxide method of preparing the hydroxy, amino and dimethylamino esters described in this/

this thesis appears to be the most rapid and satisfactory method, yet devised, of obtaining these compounds in the optically pure state. It seems to be the only way of obtaining the anthranilate and p-aminobenzoate from the corresponding acids.

In conclusion the writer desires to express his thanks to Dr H. G. Rule for his very valuable advice and interest during this investigation.